

BEDSIDE MEDICINE FOR BEDSIDE DOCTORS

An Open Forum for brief discussions of the workaday problems of the bedside doctor. Suggestions of subjects for discussions invited.

TUBERCULOUS CERVICAL LYMPHADENITIS

1. ETIOLOGY AND DIAGNOSIS

WILLIAM C. VOORSANGER, M. D. (490 Post Street, San Francisco).—Tuberculosis of the lymphatic system or nodes has engaged the attention of the medical profession for centuries. It used to be called scrofula (from the Latin scrofa, "a brood-sow"), and in the Middle Ages it was called "King's Evil," because, supposedly, it could be cured by the king's touch. Virchow was perhaps the first pathologist to recognize a really tuberculous or nodular form (of tuberculosis), of which tubercle was the unit, although he was mistaken in his conception of the true nature of the disease. Villemin was the first to advance the theory of the specific origin and infectious nature of tuberculosis even before the discovery of the bacillus by Koch in 1882.

Etiology.—During the past quarter century we have seen an astounding decrease in the incidence of lymph-node tuberculosis, in fact of all non-pulmonary forms. The reason is, of course, clear. There are three forms of the tubercle bacillus—the human, the bovine and the avian. All pulmonary tuberculosis is caused by the human form—all non-pulmonary, particularly lymph-node involvement, by the bovine; although some authors, notably l'Espérance, believe that the avian bacillus may also produce lesions in the human. With the definite knowledge that glandular tuberculosis was of bovine origin, pasteurization of milk became the first forward step as a means of keeping the bovine bacillus out of the lymphatic systems of babies and young children. Koch, in spite of his great contribution in discovering the cause of tuberculosis and thus clarifying the etiology of the disease, and making possible all of our advances of the past fifty years, nearly upset his own work by trying to prove, in 1900, that the bovine bacillus could not cause human tuberculosis. Fortunately, this was disproven, and pasteurization of milk continued. Other factors in causing decrease in the incidence of glandular tuberculosis were the testing and elimination of tuberculous cows, the more general and early removal of tonsils and adenoids, the improved methods of living, particularly the open air care of our children, the isolation, as far as possible, of open cases of tuberculosis, and the increased resistance of the white race to tuberculosis—commonly called "the white race's immunity," acquired through generations of infection with the tubercle bacillus. The almost complete disappearance of lympho-node tuberculosis in our communities through the above methods proves that the existence of these evils were the etiological factors in producing the disease.

Thirty years ago it was common to see children and later adults with "swollen glands." It was also common to see many badly-scarred necks, the sites of surgical removal of these diseased glands. True, some of these glands were inflammatory, due to diseased tonsils and adenoids, but most were due to tuberculosis. The common theory, at the beginning of the century, was that the tubercle bacillus entered the body through the respiratory tract, by aspiration or through the lymphatics by way of the intestinal tract or through the bowels. The epoch-making work in 1900 of Benda on thoracic duct tuberculosis is well known, but in later years it has been displaced by other theories. We then asserted that the bacillus remained locked up in the bronchial or hilar glands until some inciting cause, such as pneumonia, influenza, or lowered resistance caused the bacillus to leave the glands, enter the lungs and produce pulmonary tuberculosis. These theories have changed somewhat since we know more regarding childhood tuberculosis (glandular form as distinguished from massive destructive tuberculosis in the adult), and we now believe that first infection in the parenchyma of the lung may occur directly.

The decrease in the death rate from tuberculosis in general in the past twenty-five years from a high of 325 per 1,000,000 to 58 is well known. The main reduction has taken place in the age bracket, 1-10 years, and it was also in that age bracket where cervical lymphadenitis was most common. Its incidence, thanks to our now well-known preventive measures, is markedly decreased throughout the country and in certain urban communities almost nil. At the Massachusetts General Hospital the figure for the year 1931 showed only 84 new admissions of lymph-node tuberculosis as against 110 in 1925. The picture in certain outlying districts where preventive measures have fallen down is not so bright. In the southern part of California, where the Mexican population percentage is high, cervical lymphadenitis, tuberculous peritonitis and various forms of joint tuberculosis are again much in evidence, particularly in children. In certain northern counties, where raising cattle is the principal industry, I am reliably informed that bovine tuberculosis in children is again rearing its head. So the situation in the south is probably only partly due to the low resistance of Mexican children, but primarily caused, as in these northern counties, by direct infection from uncontrolled tuberculous herds. Pasteurization of milk where carried out properly should prevent bovine infection. Complete elimination of tuberculous cattle, as it has been done in most states, is an absolute preventive. California is one of the few states in the Union not demanding compulsory eradication of tuberculous cows from dairy herds. This we hope to see

remedied in the near future. Since milk and milk-products from tuberculous cows are probably the principal etiological factors in producing lymph-node tuberculosis, complete disappearance of this condition should be accomplished by the single preventive of raising cattle free of the disease.

In England there are nearly two thousand human deaths annually from bovine tuberculosis, and an incidence of four thousand new cases of bovine infection. In Ireland, "where cows are not reported unless actively sick," the situation is far worse ("Tuberculosis of The Lymphatic System," by Richard H. Miller, 1934). This country, except in isolated regions, has been fairly well purged of bovine infection in humans. We hope to keep it so!

As stated above, the direct cause of lymph-node tuberculosis is the bacillus tuberculosis bovinus which is different from the human type morphologically and culturally. It is "shorter, thicker and more regular in size, and grows in various culture media scantier than the human type." The scope of this discussion prevents further elaboration of the work done in recent years on the tubercle bacillus and its fractions by Sabin, Andersen and others.

Diagnosis.—Miller states: "The importance of tuberculosis of the lymph-nodes depends on the facts that (1) from them tubercle bacilli may be carried elsewhere in the body by lymph vessels or the blood stream and (2) they may rupture and pour caseous pus, carrying tubercle bacilli into the bronchi or gastro-intestinal tract!"

The lymph-nodes of the neck consist of two main groups, the superficial and the deep. The superficial are occipital, mastoid, parotid or pre-auricular, facial, submaxillary, submental and retropharyngeal. We also have supraclavicular glands. The superficial nodes drain into the deep or carotid or substerno-mastoid nodes, "which consist of a group of fifteen to thirty nodes lying behind the angle of the jaw, anterior to and behind the sterno-mastoid muscle, and extending down to about where the omohyoid muscle crosses under the sterno-mastoid. In addition there is another small group lying behind the posterior upper portion of the sterno-mastoid muscle and called the external group." Any of the above groups may be affected by tuberculosis actively or inactively. In pulmonary tuberculosis we can often palpate glands in the neck, but these nodes remain stationary or recede completely with improvement of the general disease. They seldom show active disease. Active infection in cervical glands is most often primary.

Tuberculous infection of cervical nodes is most frequently seen in the carotid group, located just behind and below the angle of the jaw. Next in frequency are the submaxillary and the supraclavicular. One sometimes sees a "generalized tuberculous lymphadenitis," or enlarged lymph-nodes all over the body. When a lymph-node is first infected it enlarges slowly, its center softens and it becomes caseous, and then the infection travels from gland to gland until a chain of a dozen or more may be involved. One of our objections to surgery on cervical glands, when these were commonly seen, was that often, after removal of a

chain of glands, a second chain became infected and broke down. This was no doubt due to drainage of caseous material from one chain to another. Nodes may become enlarged and caseous, but never grow to great size, and the process may calcify and heal, or absorption may take place early and only small nodular masses remain, or they may form larger knotted masses and break down. When a mass forms it often softens, breaks down, and pus and caseous material pour out. Again our scope will not permit of a detailed pathological discussion of all the phases of healing, calcification, coalescence, or caseation of tuberculous lymph-nodes. The diagnosis of the condition, although simply made, depends nevertheless upon an understanding of the underlying pathology.

When a cervical node of tuberculous origin forms, it is usually painless but worries the patient considerably. It gradually enlarges, also without pain, causing some impaired motion of the neck. The constant twisting of the neck may influence the mass and then some pain is felt. If the mass softens and becomes secondarily infected with pyogenic organisms, pain will be present. One important diagnostic feature not often present is a mild rise in afternoon temperature. In childhood tuberculosis, always of glandular origin, we are first directed to our diagnosis by afternoon rises in temperature. Sometimes the patient feels ill and tired, as in the pulmonary forms, but most often he has no general symptoms. Although symptoms are often absent, a mass in one's neck gives the patient concern, and must be diagnosed, particularly if it has a tendency to enlarge. A skin test with Tuberculin O.T. or P.P.D., if definitely positive, will show at least tuberculosis infection, not necessarily active disease. Biopsy is, of course, a sure diagnostic test. Removal of a node and finding tubercle proves our case, but the removal must be carefully performed to avoid spread of infection. The blood picture is of some help in making a diagnosis but not too characteristic. The white count is low with an increase in lymphocytes. Cunningham and Tompkins (quoted by Miller), state: "(1) Lymph-node tuberculosis gives a higher monocyte and lower lymphocyte count than is indicated by the grade of clinical severity, and (2) children tend to show higher monocyte and lower lymphocyte values than are indicated by the grade of clinical severity." The sedimentation rate, unless pulmonary tuberculosis is present, is not increased. Briefly then, enlarged lymph-nodes in the neck, particularly in young people, which are painless, break down and enlarge slowly are usually tuberculous. We must differentiate a simple lymphadenitis usually of inflammatory origin, also seldom seen, since early removal of enlarged tonsils has become a general custom. The lympho blastoma group consisting of Hodgkin's disease, lymphatic leukemia, etc., lymphosarcoma, malignancy, actinomycosis, syphilis, tumors of the parotid glands and neurofibroma are conditions of more or less frequency occurring in the cervical glands, and to be differentiated from tuberculosis in making a diagnosis. Hodgkin's disease, in its early stage, may be confused with tuberculosis, and

a generalized tuberculous adenitis with large cervical masses may be taken for Hodgkin's. The differentiation is not always easy even under the microscope. Some authors have described a Hodgkin's of tuberculous origin. The differentiation from syphilis, lymphosarcoma and malignancy should not be difficult.

In conclusion let me stress this important fact: That primary tuberculous cervical lymphadenitis as a primary disease can be almost completely eradicated, as it already has been materially reduced in incidence by the simple procedure of acquiring dairy herds free from tuberculous infection. If this is done there will be no need for diagnostic criteria for a disease which no longer exists.

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II. GLANDULAR TUBERCULOSIS

F. M. POTTENGER, M.D. (Pottenger Sanatorium, Monrovia).—Today, tuberculosis of the lymph glands is seldom seen. Since people live more hygienically, and patients are treated with greater care, all of the complications of this disease have been reduced in frequency and severity.

The reduction in the amount of glandular tuberculosis may be partly due to this same cause. On the other hand, it is partly due to the improvement in milk supply. It is generally admitted by pathologists that many of the nonpulmonary tuberculous lesions are caused by the bovine bacillus which is transmitted through milk; and since the danger of infection has been removed to so great a degree from milk, all of these types of the disease are disappearing.

Tuberculosis of the glands of the submaxillary group is the glandular infection which most commonly assumes clinical importance. The submental and posterior cervical are less commonly, and the axillary and inguinal rarely, involved. Where submental glands are involved in acute inflammation it is most apt to be of a nontuberculous infection, the origin of which lies in the oral cavity.

The symptomatology of acute infection of the cervical glands and of tuberculous infection is very similar. Both show swelling, which is often painful in the early stages, before softening occurs. Swelling and pain are practically always present in the nontuberculous gland. Fever may be present in either instance.

Tuberculosis of the anterior cervical glands usually shows slow swelling, is at least comparatively painless, and sometimes wholly so. Usually more than one gland is involved. When several glands are involved, they show different degrees of enlargement. As time goes on the skin over the tuberculous gland usually becomes adherent. Caseation and rupture come on slowly after the gland has been enlarged for some time. In acute infection suppuration usually occurs much more quickly.

It may be difficult to find tubercle bacilli in the pus from the tuberculous gland. As a rule, however, if concentration methods are used, they will be found.

Tuberculous glands must also be differentiated from lymph granulomata. The latter do not be-

come adherent to the skin, nor do the glands rupture and form fistulous tracts.

It must be remembered that tuberculosis of the lymph glands can come either as a complication of tuberculous disease elsewhere in the body, especially that in the lung, or it can come as a separate organ involvement. In both instances the source of infection is usually by way of the blood stream, the infection of the gland taking place in the same way that a bone, joint or kidney becomes infected.

Pathologists, however, recognize the possibility of infection through the mucous membrane of the oral cavity by bacilli which come from the lung, and lie in contact with the mucous membrane of the mouth and throat.

This infection is similar to such infections in the larynx and intestinal tract which are recognized as taking place through contact. It is probable, however, that this method of infection is less frequent than that by way of the blood stream.

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III. ROENTGEN RADIATION THERAPY

ALFRED C. SIEFERT, M.D. (411 Thirtieth Street, Oakland).—Twenty-five years ago the treatment of tuberculous cervical lymphadenitis was still overwhelmingly surgical, although as early as 1905 roentgen-radiation therapy was being advocated by many of the pioneer roentgen therapists at home and abroad. In this country we may name, in this connection, Williams and Pusey, Pfahler, Rodman, and others, while abroad the names of Holzknecht, Kienboeck, and Wetterer, also Bergonie, and a little later Bargon and Béclère and many others, who advocated and praised the efficacy of roentgen therapy.

The most complete individual discussion which the writer could find in the literature on the subject in hand was still to be found in the third edition of Wetterer's "Handbuch der Roentgen und Radium Therapie," 1920. Since then one may find a number of casual references to the matter in the journalistic literature.

While surgery is entirely efficient, as well as sufficient, when the affected glands are still small, few in number, and superficially located so that the disease can be entirely removed, it ceases to be efficient when the affected glands are numerous and the disease is advanced, and the deeper cervical glands are affected, or when the glands have coalesced into conglomerations of tuberculous lymphomata, or have broken down to form pus and tuberculous fistulae, such as one sees even in this day and age all too frequently. The cosmetic results in such cases are usually poor with surgery, and repeated surgical intervention becomes necessary and increasingly difficult, and, furthermore, there is no assurance that the disease can be completely controlled. In contrast to this, it may be argued with justification that, even in advanced and neglected cases, roentgen irradiation offers, in a very high percentage of such cases, a complete cure with much better cosmetic results. The cosmetic effects are, of course, especially gratifying when the patient can be taken in hand at an early stage of the disease, roentgentherapeutically.

From an immunological point of view, one may state that the roentgen treatment is much more satisfactory than any other, for the reason that the body forces are mobilized to combat the disease and, in so doing, immune substances are created of considerable value. It is the consensus of well founded opinion and experience that the tubercle bacillus is not primarily affected by roentgen radiation in therapeutic doses. It is rather the necrobiosis of radiated tuberculous tissue which causes the liberation of tuberculo-toxins which, in turn, stimulate the formation of immune substances in the organism, promote phagocytosis, and induce proliferation of connective tissue. The ultimate result is, accordingly, the gradual resorption of the diseased tissue and its replacement by fibrous tissue, or, in rarer instances, the deposit of lime salts in the diseased tissue, such as is frequently observed in childhood tuberculosis of the lungs, when both the primary lesion, and the secondary hilum and mediastinal lymph glands have undergone spontaneous healing. In the more-advanced cases of tuberculous cervical lymphadenitis, the first action of irradiation is upon the acute periadenitis, with the result that the chronically diseased glands become again discreet and isolated, after having formed a coalescence of involved glands. Similarly, glands that have broken down with the formation of tuberculous fistulae, may be so influenced by irradiation so as to bring about a cessation of discharge and a closure of the discharging sinuses.

The further discussion of these topics will be resumed below.

At this time a few words may be introduced concerning objections which formerly might have been brought against roentgen therapy and which still are occasionally mentioned. These objections are, notably, undesirable effects on the radiated skin, such as atrophy of its glands and appendages, and subsequently the formation of unsightly telangiectases and occasionally even more serious late sequelae. It may be said today that such objections are no longer tenable, in consideration of the efficiency of modern apparatus, and the use of heavy metal filters such as copper or zinc. During the last ten to twelve years the writer has used routinely $\frac{1}{2}$ to 1 mm. of copper as a filter for x-radiation, and during this time has observed none of the disagreeable sequelae that sometimes followed the use of roentgen radiation, filtered through aluminum, even through rather heavy thicknesses, and this in spite of all care and skill. Nevertheless, it must be urged that even today the treatment of tuberculous glands of the neck by roentgen radiation is not a task for the amateur or the occasional roentgen-therapist, and the best results may only be expected from one who has had plenty of experience.

Tuberculous lymphadenitis must be treated with small doses of radiation, and these repeated at not too frequent intervals. The only exceptions to this general statement are such glands in which the disease is so advanced that a breaking down and liquefaction of formidable masses of tuberculous tissue are manifestly inevitable. In such cases it is better to give a larger dose at one sitting in order to

hasten liquefaction, and as soon as fluctuation is perceptible, and, before the overlying skin has become reddened and thin, to evacuate the tuberculous abscess, if possible, by means of aspiration of the pus through a large bore needle, or if this be impossible, on account of large, cheesy masses, through incision with a pointed scalpel. It is well, in most cases, if the abscess be incised, to pack it for a short time with a wick of iodoform gauze before the fistula is allowed to close. The breaking down and liquefaction of glands with abscess formation is no contra-indication to the continuance of roentgen therapy. On the contrary, the treatment should proceed without further modification. For the benefit of those who may be interested, the following details of the writer's treatment technique are given.

In the average case, a dose of 100 to 150 international roentgen units, measured on the skin with backscatter, are given under the following conditions: KVP 180—MA 20—Target skin distance 60 cm.—Filter 1 mm. of copper plus 1 mm. of aluminum. Intensity is approximately 20 R per minute. The effective wave length under these conditions lies between 0.14 and 0.13 Ångstrom units. The half-value layer is approximately 1.47 mm. of copper. The field is somewhat variable according to the age and size of the individual treatment, varying from 100 to 150 or more square centimeters. It is best to direct the central ray tangentially to the neck so as to avoid, as much as possible, the irradiation of normal structures. For shielding, the writer uses a piece of sheet lead approximately 30 cm. square. The lead should be sufficiently thin so that it may be readily molded to the contours of the patient's neck. An opening is cut out of the sheet lead in the shape of a trapezium. The longer parallel side of the trapezium runs along the median border of the sternocleidomastoid muscle. The posterior shorter parallel side runs along the line of the spinous processes of the cervical column. The inferior side runs along the clavicle and the superior just skirts along the tip of the mastoid process below the hair line. The size of this opening may be varied according to needs by additional lead strips. If an active tuberculosis be present in the apex of one of the lungs, it is important to shield the supraclavicular fossa. It is evident that the larynx is always well protected. The treatments, as outlined above, are repeated at intervals of three to four weeks, until a cure has been effected, although caution is to be urged when the number of treatments begins to exceed ten to twelve. As already stated, greater doses at shorter intervals may be given if a rapid liquefaction of tuberculous tissue is to be brought about.

As to possible contra-indications to roentgen therapy, the question is frequently asked by colleagues, unfamiliar with radiation treatment, whether or not the thyroid and parathyroid glands may be adversely affected. The writer has never observed hypothyroidism or hypoparathyroidism following therapeutic irradiation of tuberculous glands of the neck, and has not come across anything in literature which would indicate that such a danger is real. Moreover, all those who have

treated thyrotoxicosis with roentgen radiation are aware that even in a state of hyperplasia the thyroid gland is relatively resistant to the action of the rays, and it follows, logically, that the normal thyroid gland is even more resistant. The same considerations apply to the parathyroid.

Where the ridiculous notion has arisen that radiation therapy applied to the neck might affect the ovaries of female children, which the writer has heard brought up in all seriousness in this journal, is difficult to understand. That such a thing has no foundation, in fact or experience, is here stated with emphasis once and for all. The only real danger to be avoided is the unwanted radiation of active tuberculous lesions in the apices of the lungs, as has already been brought out, but this danger cannot be overemphasized.

Concerning the diagnosis of tuberculous lymphadenitis of the neck, a few observations are of importance in connection with its treatment. It is always, of course, desirable, when any therapeutic agent is employed, to have the diagnosis as definitely established as is possible. There are, however, some conditions where the differentiation between tuberculous lymphadenitis and other lymphadenopathies is not immediately possible. In such cases, resection of the gland and biopsy may be desirable, but in many instances, irradiation itself serves as a diagnostic procedure. Thus, the lymphadenitis in connection with acute or subacute, or even chronic infection of the throat, tonsils, etc., shows, following the first irradiation, a marked swelling of the individual glands, an elevation of temperature which is characteristic and does not, as a rule, take place when the glands are tuberculous. Such glands are favorably influenced by roentgen treatment, and usually the regression in size is rapid, a return to normal being accomplished in one to two weeks, which is never the case with tuberculous glands, except, perhaps, in a very early and acute stage, and then such regression may be regarded as a favorable sign from a prognostic point of view.

In case of lymphatic leukemia, the differentiation is readily made on the blood count and the smear, also by the fact that usually the disease is disseminated through various groups of glands accessible to palpation or fluoroscopy, notably the axillary and inguinal groups, as well as the mediastinal group. They respond readily to radiation therapy by shrinking and even completely disappearing, but a relapse takes place with equal readiness. In Hodgkin's disease, the blood count may leave one in doubt, but here, too, as a rule, more than one group of glands is involved, and the response to radiation is almost equally rapid. Occasionally, however, it may be necessary to excise a gland for microscopic examination to establish the diagnosis of Hodgkin's disease. Much more rarely will the cervical lymph glands be the site of metastases of malignant neoplasm where the primary neoplasm may be obscure. The author, however, has had the experience where a bronchogenic carcinoma located in the apex of the right lung was mistaken, temporarily, for an apical tuberculosis, and only the resection of a palpable cervical gland with the

biopsy finding of carcinomatous metastasization led to the correct diagnosis.

Finally, it remains to discuss the prognosis in roentgen treatment of tuberculous glands of the neck and to state the criteria of a cure. The prognosis may be said to be very good, and the writer's experience would place the percentage of favorable results as high as 90 per cent. The criteria of a complete cure are, first of all, the shrinking of the glands with the production of firm fibrous nodules, which may be felt in place of the diseased glands and are usually described as "shot-like," resembling, as they do, bird shot. Tuberculous abscesses completely heal and all discharge ceases, and fistulae close and remain closed. Unsightly scars may then be resected surgically. It is well to observe the patient for months or even for a year or more after treatment has ceased, in order to see that all criteria of a cure have been well established.

Occasionally it happens that a gland will become firm and hard, but will not shrink. Such glands it has been the author's custom to have resected by a surgeon. The finding is usually tuberculous tissue, caseous or liquefied, surrounded by a thick, dense fibrous shell. This dense fibrous coat effectively chokes off the tuberculous disease and renders the gland thus changed a poor soil for the tubercle bacillus to live and grow. To be sure, it cannot be absolutely denied that tubercle bacilli may remain alive in such an altered gland for a considerable period of time, but their dissemination is effectively barred. Nevertheless, the resection of this type of gland is desirable. More commonly, however, the diseased glands are changed, as has already been stated, into small dense, hard, fibrous bodies, in which the tuberculous disease has been completely eliminated, and which forms a criterion of successful treatment.

The National Health in Japan.—In the present session of the Imperial Diet, Mr. Hasama, Chief of the Board of Health, discussed the health of the Japanese nation. The present inclination of the birth rate is slightly downward, but it is high in comparison with that of other countries, being thirty per thousand of population. The higher rates are found in the northern provinces, and the lower rates in the larger cities and the middle parts of the country. The death rate was 18.1 per thousand in 1934. More than 130,000 persons died of tuberculosis in 1934, the rate being 19.3 per 10,000 of population, including more than 96,000 persons who died of pulmonary tuberculosis. There were about 49,000 cases of dysentery in 1935, seven per 10,000 of population, and more than 15,000 deaths. According to the investigation made by the home office, of 152,050 villagers who were examined by the official experts, 118,000, about 78 per cent, had infestation with some kind of parasite. There are reported to be more than 7,000,000 cases of trachoma throughout the country. The number of insane increased and was greater than 83,000 in 1935. Venereal diseases also increased. The physical examinations of conscripts revealed that the number of those who fail the medical tests are regularly increasing every year throughout the country. The cause, however, is not clear. The home office has planned to establish this year as many health centers as possible in all parts of the country.

Our country can probably boast of no more courageous a set of heroes than her gallant men who bend over her laboratory test tubes; the sword of science is at constant duel with the physical demons that plague mankind.